MODERN DEVELOPMENTS OF HARVEY'S WORK.

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DR. LAUDER BRUNTON.

MODERN DEVELOPMENTS OF HARVEY'S WORK.

THE

HARVEIAN ORATION

1894

DELIVERED BEFORE

THE ROYAL COLLEGE OF PHYSICIANS

OCTOBER 18TH, 1894

BY

T. LAUDER BRUNTON, M.D., F.R.S.

FELLOW OF THE COLLEGE;

ASSISTANT PHYSICIAN TO ST. BARTHOLOMEW'S HOSPITAL

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TO

J. RUSSELL REYNOLDS, M.D., F.R.S.,

PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS,

PHYSICIAN IN ORDINARY TO HER MAJESTY'S HOUSEHOLD,

THIS ORATION,

DELIVERED AT HIS DESIRE,

IS DEDICATED

WITH PROFOUND RESPECT AND KIND REGARDS.

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THE HARVEIAN ORATION, 1894.

By T. LAUDER BRUNTON, F.R.S.

Mr. President, Fellows, and Gentlemen,

This annual meeting in memory of Harvey is usually associated with feelings of pleasure and happiness, for it was intended by its immortal founder to commemorate the benefactors of the College and to encourage good fellowship amongst us.

Such commemoration of those who have benefited the College in the past, although it necessarily recalls many who have passed away, is, notwithstanding, on ordinary occasions pleasant instead of painful, because the feeling of loss through their death is completely overpowered by the recollection of the good they have done in their lifetime. To-day the case is very different, for the first thought that must needs occur to every one present here is that on this occasion last year our late President showed for the first time what seemed to be imperfect fulfilment of his duty to the College by being late in his attendance at the meeting. Perhaps nothing else could have shown more clearly his deep concern for the welfare of the College, and his thorough devotion of every faculty of mind and body to its interests, than the fact that no duty, no pleasure, and no press of occupation could tempt him to leave one iota of his work in the College undone. The only thing that did keep him back was the hand of Death, which, although at the last meeting he and we knew it not, was already laid upon him. Though his death was less happy than that of the great Harvey, inasmuch as he

lingered on for days instead of hours after he was first struck down, yet their deaths were alike in this respect that, up to the time of the fatal attack, each was in the full possession of his faculties, each was in the enjoyment of his life. Like Radcliffe and Mead, like Halford and Baillie, and like many other distinguished Fellows of this College, the greatness of Clark is to be estimated not by the published works which he has left behind, but by the influence he exerted on his contemporaries. For the very estimation in which his professional skill was held led to his whole time being taken up in giving advice, and prevented him from having the leisure to work out or record the results of the pathological and clinical observations which both his useful publications and his later career showed him to be specially fitted to make. I might say very much more about him, but it has already been said much better than I could possibly do it by yourself Mr. President, in your annual address, and in the eloquent and heart-stirring words which you addressed to the College on the occasion of your taking the presidential chair rendered vacant by the death of Sir Andrew Clark..

But while we are saddened by the death of our late President, we hope to be gladdened by the presence amongst us again of one whom we all reverence not only as a former President of this College, but as one of the greatest leaders of clinical medicine in this century, Sir William Jenner. Like Harvey, Sir William Jenner is honoured by his College, by his country, by his Sovereign, and by the world at large. In time of trial and danger the lives of the Royal children were committed to the keeping of Harvey by his King; and to-day the care not only of her own life, but of that of her nearest and dearest, is committed to Sir William Jenner by his Sovereign, in the full and well-grounded assurance that in no other hands could they be more safe. The great clinician, Graves, wished to have as his epitaph "He fed fevers"; but

Jenner has advanced much beyond Graves, and, by showing us how to feed the different kind of fevers, has saved thousands of valuable lives. To-day this College is acknowledging his right to rank with Sydenham, Heberden Bright and Garrod, by bestowing upon him the Moxon medal for clinical research. In numbering Sir William amongst its medallists, the College honours itself as wel as him, and in acknowledging the great services he has rendered, it is, on this occasion, acting as the mouth-piece of the medical profession, not only in this country but in the world at large.

It was with the wish to keep green the memory of the benefactors of the College that this oration was instituted by Harvey, and not at all with the intention that it should be devoted to his own praise. But Harvey stands out so high above all others, that it is only natural that in the numerous orations which have been yearly given before the College of Physicians, the subject matter should have been to a great extent confined to a consideration of Harvey and his works. On looking over many of these orations, I find that everything that I could say about Harvey, his person, his circumstances, his character, and his works, has already been said so fully and eloquently that I could not add to it any further, nor could I hope to express it even so well. I purpose, therefore, to consider to-day some of the modern developments of Harvey's work, more especially in relation to the treatment of diseases of the heart and circulation. There is, I think, a certain advantage in this also, inasmuch as one is apt, by considering Harvey's work only as he left it, to overlook the enormous extent to which it now influences our thoughts and actions; and thus to comprehend its value very imperfectly.

As he himself says, "From a small seed springs a mighty tree; from the minute gemmule or apex of the acorn, how wide does the gnarled oak at length extend his arms, how

loftily does he lift his branches to the sky, how deeply do his roots strike down into the ground!"[1]

How very minute is the gemmule from which has sprung everything that is definite in medical science, for this gemmule is no other than the idea which Harvey records in in these simple words: "I began to think whether there might not be A MOTION AS IT WERE IN A CIRCLE."[2]

Out of this idea has grown all our knowledge of the processes of human life in health and disease, of the signs and symptoms which indicate disease, of the mode of action of the drugs and appliances which we use, and the proper means of employing them in the cure of disease. In the works that have come down to us, we find that Harvey developed his idea physiologically in several directions. He discussed its application to the absorption and distribution of nourishment through the body, the mixing of blood from various parts, the maintenance and distribution of animal heat, and excretion through the kidneys. How far he developed it in the direction of pathology and therapeutics we do not know, as the results of his labours on these subjects have, unfortunately, been lost to us by the destruction of his manuscripts during the Civil War.

We are proud to reckon Harvey as an Englishman by birth, but he is far too great to belong exclusively to any country; men of various nations and scattered all over the face of the earth acknowledge him as their teacher, and have played, or are playing, a part in developing his discovery in its various branches of physiology, pathology, pharmacology, semiology, and therapeutics. Americans, Austrians, Danes, Dutchmen, French, Germans, Italians, Norwegians, Russians and Swedes have all shared in the work, and so numerous are they that it would be impossible for me to name them all. Stephen Hales, however, deserves special mention, for he was the first to measure the pressure

[1] "The Works of W. Harvey," Sydenham Society's edition, p. 320.
[2] *Ibid.* p. 46.

of blood in the arteries, and the resistance offered to the circulation of the blood by the capillaries was investigated by Thomas Young, a Fellow of this College, who ranks with Harvey, Newton, and Darwin as one of the greatest scientific men that England has ever produced, and whose undulatory theory has been as fertile of results in physics as Harvey's idea of circulation has been in physiology and medicine.

Harvey's desire that those who had done good work should not be forgotten was founded upon his knowledge of mankind, and of the tendency there is to forget what has already been done by those who have gone before us. The opposite condition often prevails, and the past is glorified at the expense of the present. But sometimes the present is wrongly glorified at the expense of the past, and past work or past benefits are forgotten.

Good examples of this are afforded by physiological views regarding the action of the vena cava and pulmonary veins and the causation of the cardiac sounds. Harvey appears to have thought that the vena cava and pulmonary veins were simply dilated passively by the passage of blood into them; but the fact that they possess a power of independent pulsation was known to Haller,[3] and was brought prominently forward by Senac,[4] who regards the vena cava as the starting-point of the whole circulation. He says: "The vena cava is therefore the first motor cause which dilates the cavities of the heart; it fills the auricles, and extends their walls in every direction."

These observations appear to have been almost forgotten until they were again made independently a few years ago,[5] and in one of the latest and most accurate physiological treatises which now exist, the description of the cardiac

[3] Haller, "Elementa Physiologiæ," 1757, tome I, pp. 410 and 399.
[4] Senac, "De la Structure du cœur," livre iv., ch. iii., p. 24.
[5] *Proc. Roy. Soc.*, 1876, No. 172.

cycle is nearly the same as that given by Senac. "A complete beat of the whole heart, or cardiac cycle, may be observed to take place as follows:

"The great veins, inferior and superior venæ cavæ and pulmonary veins are seen, while full of blood, to contract in the neighbourhood of the heart; the contraction runs in a peristaltic wave towards the auricles, increasing in intensity as it goes."[6]

The pulsation of these veins, however, cannot be a constant phenomenon, or it would have been noticed by such a keen observer as Harvey.

The sounds of the heart were discovered by Harvey, or at least were known to him, for he speaks of the sound caused in the œsophagus of the horse by drinking, and says, "In the same way it is with each motion of the heart, when there is a delivery of blood from the veins of the arteries that a pulse takes place and can be heard within the chest."[7]

This observation remained, as far as we know, without any further development until the time of Laennec, who introduced the practice of auscultation; but it was a Fellow of this College, Dr. Wollaston,[8] who first discovered that muscles during contraction give out a sound. Although many observations were made regarding cardiac murmurs by Corrigan, Bouillaud, and Piorry, it was chiefly by Fellows of this College, Dr. Clendinning, Dr. C. J. B. Williams, and Dr. Todd, that the question was finally settled, and the conclusions at which they arrived are those now accepted as correct, viz. that "the first or systolic sound is essentially caused by the sudden and forcible tightening of the muscular fibres of the ventricle when they contract; and that the second sound which accompanies the diastole of the ventricle depends solely

[6] M. Foster, "Text-book of Physiology," 6th edition, part i., ch. iv., p. 231.

[7] Harvey's Works, Sydenham Society's Edition, p. 32.

[8] Wollaston, "Phil. Trans." 1810, p. 2.

on the reaction of the arterial columns of blood in the semilunar valves at the arterial orifices."[9]

Yet in recent discussions regarding the origin of cardiac sounds, little mention has been made of the work of this committee; and, indeed, I first learned of its value from a German source, viz: Wagner's "Handwörterbuch der Physiologie."

The importance of these observations in the diagnosis of heart disease it would be hard to over-estimate. But diagnosis alone is not the aim of the physician, whose object must be to prevent, to cure, or to control disease. A knowledge of physiology may greatly help us to prevent disease, not only of the heart and vessels, but of every member of the body. The control and cure of disease may also be affected by diet and regimen, but it is undoubtedly in many cases greatly assisted by the use of drugs, and is sometimes impossible without them. Harvey knew that drugs applied externally are absorbed and act on the body,[10] so that colocynth thus applied will purge, and cantharides will excite the urine; but the action of drugs when injected into the blood appears to have been tried first by Christopher Wren, better known as the architect of St. Paul's than as a pharmacologist. According to Bishop Spratt, "he was the first author of the noble experiment of injecting liquors into the veins of animals, an experiment now vulgarly known, but long since exhibited to the meetings at Oxford, and thence carried by some Germans, and published abroad. By this operation divers creatures were immediately purged, vomited, intoxicated, killed, or revived, according to the quality of the liquor injected. Hence arose many new experiments, and chiefly that of transfusing blood, which the Society has presented

[9] Report of Committee consisting of C. J. B. Williams, R. B. Todd, and John Clendinning, "Brit. Ass. Rep. for 1836," p. 155.

[10] "The Works of William Harvey," Sydenham Society's edition, p. 72.

in sundry instances, that will probably end in extraordinary success." [11]

The method originated by Wren, of injecting drugs into the circulation, was skilfully utilised by Magendie for the purpose of localising the particular part of the body upon which the drugs exerted their action, and he thus conclusively proved that the symptoms produced by strychnine were due to its effect on the spinal cord. His experiments showed that the rate of absorption from various parts of the body varied enormously, and through the teaching of Christison, led to the introduction into practice by Dr. Alexander Wood of that most useful aid to modern therapeutics, the hypodermic syringe.

The first quantitative experiments on the effect of drugs upon the circulation were made, to the best of my knowledge, by James Blake in 1844, in the laboratory of University College, at the suggestion of the late Professor Sharpey, with the hæmodynamometer of Poiseuille, which had then been recently introduced.

In speaking about the work of Blake and Sharpey, who are both dead, one requires to use the greatest care not to unduly detract from the merit of one by ascribing more to the other; but those who knew Prof. Sharpey's enormous range of knowledge, his readiness to put it all at the disposal of others, and the influence he exerted over all who came in contact with him, as well as his unselfishness in making no claim whatever to what was justly his due, will at once recognise how greatly Blake was indebted to Sharpey. More especially is this the case when we consider that, although the credit for the observations themselves belongs to Blake, yet after the impetus which Sharpey gave him had passed away, he did very little more during the course of a long life. It seems all the more necessary to commemorate Sharpey on this occasion,

[11] "The History of the Royal Society of London for the Improving of Natural Knowledge," by T. Spratt, late Lord Bishop of Rochester.

because he has left comparatively few writings behind him, and anyone who should judge by them alone of his influence upon physiological progress in this country would greviously under-estimate it. For Sharpey was above all a teacher, and his work was written not with pen and ink on paper or parchment, but was engraved upon the hearts and minds of his pupils and his friends. Upon two of these, especially, has Sharpey's mantle fallen, and to Burdon Sanderson and Michael Foster we owe a revival of experimental physiology in this country, a revival of the method which Harvey not only used in making his great discovery, but also employed to demonstrate the truth of it to the rulers of this land. By their writings, by their lectures, by their original experiments, by their demonstrations, and by the pupils they have trained, Burdon Sanderson and Michael Foster, under the auspices of Acland and Humphry, have diffused amongst the medical men of this country a knowledge of physiology so extensive and exact as could only be found, before their time, amongst those who had made a special study of the subject. Yet more than to them, more than to anyone else since the time of Harvey, do we owe our present knowledge of the circulation to Carl Ludwig. He it is who first enabled the pressure of blood in the arteries to record its own variations automatically, so that alterations could be noticed and measured which were too rapid or too slight to be detected by the eye. To him, also, we owe the plan of artificial circulation by which the changes in the functions of the organs and in the vessels which supply them can be observed, quite apart from the heart, lungs, or from the nervous system.

Like Sharpey, Ludwig is a great teacher, and, like the great architects of the Middle Ages, who built the wonderful cathedrals which all admire, and whose builder's name no man knows, Ludwig has been content to sink his own name in his anxiety for the progress of his work, and in his desire to aid his pupils. The researches which have

appeared under these pupils' names have been in many instances, perhaps in most, not only suggested by Ludwig, but carried out experimentally with his own hands, and the paper which recorded the results finally written by himself. In the papers which have appeared under his pupils' names we find their obligation to the master recorded in such terms as "unter Mitwirkung." But no one, except those who have worked with him, can understand what such "co-operation" meant.

The graphic method introduced by Ludwig for the purpose of measuring the blood pressure, was adapted by Volkman to the registration of the pulse in man, and the same method has been modified and rendered more easily applicable at the bedside by Marey and Chaveau, to whom we chiefly owe our knowledge of the modifications in the form of the apex beat, and of the pulse curve. It is to Ludwig and his scholars, however, that we owe the greater part of our knowledge of the mechanism of the circulation and of the varying distribution of the blood in various parts of the body.

The effect of emotion upon the heart was carefully noted by Harvey, who says; "For every affection of mind which is attended with pain or pleasure, hope or fear is the cause of an agitation whose influence extends to the heart.[12]

Not only was Harvey well acquainted with the fact that the beats of the heart vary very much in strength and force, but he also knew that the circulation in various parts of the body may be very different at one and the same time. He says: "It is manifest that the blood in its course does not everywhere pass with the same celerity, neither with the same force in all places, and at all times, but that it varies greatly according to age, sex, temperament, habit of body, and other contingent circumstances, external as well as internal, natural, or non-natural. For it does not course through intricate and obstructed passages with the same

[12] "The Works of William Harvey," Sydenham Society's edition, p. 70.

readiness that it does through straight, unimpeded, and pervious channels. Neither does it run through close hard and crowded parts with the same velocity as through spongy, soft, and permeable tissues. Neither does it flow with such swiftness when the impulse (of the heart) is slow and weak, as when this is forcible and frequent, in which case the blood is driven onwards with vigour, and in large quantity."

"And what, indeed, is more deserving of attention than the fact that in almost every affection, appetite, hope, or fear, our body suffers, the countenance changes, and the blood appears to course hither and thither. In anger the eyes are fiery and the pupils contracted; in modesty the cheeks are suffused with blushes; in fear, and under a sense of infamy and of shame, the face is pale, but the ears burn as if for the evil they heard or were to hear; in lust, how quickly is the member distended with blood and erected,"[13]

Harvey's great contemporary, Milton, though so violently opposed to him in politics, would certainly not remain in ignorance of Harvey's work, and he has noted the changes in the colour of the face produced by emotions. In describing the behaviour of Satan on his journey from Hell to Paradise, he says :—

> "Thus while he spake, each passion dimm'd his face,
> Thrice changed with pale, ire, envy, and despair;
> Which marr'd his borrow'd visage."[14]

But although these facts were known to Harvey so long ago, it is only in comparatively recent years that the mechanism by which they are brought about has been investigated, and it is only within the last decade that physiologists have begun regularly to believe that the cardiac muscle has a power of rhythmic pulsation independent of its nerves, although Harvey had noted that when the heart

[13] "The Works of William Harvey," Sydenham Society's edition, p. 128-129.

[14] "Paradise Lost," by John Milton, Book iv.

was cut into small pieces the fragments would still continue to pulsate.[15] We may fairly, indeed, compare the movements of the heart, as regarded by physiologists of the present day, to those of a horse which is capable of going independently, although its pace may be slowed or accelerated by the reins or spur of the rider. The power of the vagus to act as a rein to the heart, and slow its movements or stop them altogether, was first noted by Edward and Ernest Heinrich Weber, while the effect that it sometimes has of accelerating instead of slowing, like the effect of shaking the reins of the horse, was observed by Schiff, Moleschott, and Lister, and the transmission of excitation from one chamber to another was experimented on by Paget.

The accelerating nerves of the heart, and the position of the nerve-centre from which they spring, were more thoroughly investigated by von Bezold,[16] while the power of the vagus to weaken as well as slow the heart was observed by Gaskell. The position of the cardiac centre, which, like the rider, regulates the movements of the heart, was located in the medulla oblongata chiefly by Ludwig and his scholars. Like the heart, the vessels are regulated in diameter by the nervous system in accordance with the wants of the body generally; and the effect upon the vaso motor nerves which, when cut, allow them to dilate, and when stimulated cause them to contract, was discovered by Bernard, Brown-Séquard, and by our countryman, Waller; while the power of other nerves to cause immediate dilatation was discovered by Bernard, Eckhardt, and Ludwig, in the submaxillary glands, penis, and peripheral vessels respectively.

The heart, when cut out of the body, still continues to beat, although removed completely from the influence of the central nervous system, and the vessels have a somewhat

[15] Harvey's Works, Sydenham Society's edition. p. 28.

[16] Von Bezold "Untersuchungen über die Innervation des Herzens," 1863. Leipzig: Engelmann.

similar power of independent contractility. The alterations produced in the circulation, generally and locally by the contractile power of the vessels, and the changes caused in the vessels by the central nervous system, by peripheral stimulation of the nerves, or by variations in the quality of the blood, have formed the subject of a series of researches extending over many years; and though originated, and in many cases entirely conducted by Ludwig, have appeared to a great extent under the names of his pupils. The starting-point of these investigations was an examination of the changes in blood as it flowed through isolated organs, with the view of ascertaining in what manner the combustion by which the animal heat is maintained is effected in the body. While keeping up the circulation of blood through the vessels of muscles severed from the body, Ludwig and Sczelkow[17] observed variations in the flow which appeared to indicate contractile power in the vessels themselves. This research was carried on under Ludwig's direction by various of his scholars in succession, Alexander Schmidt, Dogiel, Sadler, myself, Hafiz, Lépine, A. Mosso, von Frey, and Gaskell. Their observations, as well as those of Cohnheim and Gunning, have shown that the muscular fibres of the arterioles, not only in the muscles but throughout the body generally, have a power of independent, and sometimes rhythmical, contraction and relaxation. Their contractility is, however, controlled by the central nervous system in accordance with the wants of the body generally. For the amount of blood contained in the body is insufficient to fill the whole of the vascular system at once; and when the vessels are fully dilated, as they are after death, we find that nearly the whole of the blood of the body may be contained in the veins alone. It is, therefore, necessary that when one part of the body is receiving a larger supply of blood, another should be

[17] Ludwig and Sczelkow, "Henle and Pfeuffers Zeitschrift," 1863, vol. 17, p. 106 and *vide* p. 122.

receiving a smaller supply; and the functions of the vaso-motor centres have been well compared by Ludwig to the turncocks in a great city, who cut off the water supply from one district at the same time they turn it on to another. Thus it is that when the brain is active the feet may get cold, and Mosso has shown this in an exceedingly neat manner by placing a man on a large board delicately balanced at its centre, and demonstrating that whenever the man begins to think, the increased supply of blood to his brain causes the head to go down and the heels to rise up. A similar condition was indicated by Mayow, who gave a different explanation. He said that the vital spirits were not able to be in more than one place at once, and therefore it happens that if a man eats a heavy meal, he is apt to become drowsy, because the vital spirits descend from the brain to the stomach in order to carry on digestion; and, on the other hand, if a man thinks vigorously after dinner, the vital spirits have to leave the stomach to go to the brain, and consequently digestion is imperfectly performed. If we substitute the word blood for vital spirits, we have an exact expression of present physiological ideas.

Ubi stimulus ibi affluxus is an old doctrine and expresses a great truth. Wherever the need for increased nourishment or increased supply of oxygen exists in the healthy body, thither does the blood flow in larger quantities than usual. If the glands are active, their blood supply is greatly increased, as was shown by Bernard, and a similar occurrence takes place in the contracting muscle, as has been shown by Ludwig and his scholars. The vessels of the intestines and skin, as well as their numerous glands, have their calibre regulated by the vaso-motor nerves which proceed from the centre in the medulla oblongata. This centre acts most readily upon the vessels of the intestine, and rather less readily on those of the skin. In consequence of this, when the centre is irritated, the

vessels of the intestine contract and drive the blood through the skin, so that it is warmer than before, and it is only when the stimulation is very great that the vessels of both contract so that the skin receives less blood than normal, and becomes colder than before. But if the vessels of the skin and intestine are both contracted, where does the blood go? This question was put by Ludwig, and answered by the experiments which he made with Hafiz. It is evident that if the heart be stopped while the blood pressure is being measured in the artery of an animal, the pressure will fall regularly and steadily, because the blood is flowing out all the time through the arterioles and capillaries into the veins. One would naturally expect that if the arterioles were contracted by irritation of the vaso-motor centre in the medulla, the fall of blood pressure would either not take place at all, or would be very much slower than before; but on trying the experiment, Ludwig and Hafiz found, to their surprise, that the blood pressure fell almost as quickly as when the vaso motor centre was left alone and the vessels of the skin and intestine therefore remained uncontracted. In other words, the vessels which supply the muscles of the body and limbs are capable of such extension that when fully dilated they will allow the arterial blood to pour through them alone nearly as quickly as it usually does through the vessels of the skin, intestine, and muscles together. This observation, it seems to me, is one of the greatest importance, and one that has hardly received, as yet, the attention which it merits. One consequence of it is obvious—viz., that contraction of the cutaneous vessels, such as occurs upon exposure to cold, will drive more blood through the muscles, and as oxidation goes on more rapidly in them the result will be increased production of heat.

The experiments I have just mentioned show that the vessels of the muscles are not controlled by the vaso motor

centre in the medulla oblongata in the same way as those of the intestine and skin. How far their vascular centres may be associated with those for voluntary movements, which have been so admirably localised by Ferrier in the cerebral cortex, still remains to be made out. The circulation through the muscles is indeed a complex phenomenon, and it was shown by Ludwig and Sadler to depend upon at least two factors having an antagonistic action. When a muscle is thrown into action, it mechanically compresses the blood vessels within it, and thus tends to lessen the circulation through it, but at the same time the stimulus which is sent down through the motor nerve, and which calls it into action, brings about a dilatation of the vascular walls, and thus increases the circulation through the muscle.

When the amount of blood is measured before, during, and after stimulation of the motor nerve, it is sometimes found that the flow is diminished, at others that it is increased. This difference depends upon the comparative effect of the mechanical compression of the vessels of the muscles just mentioned, and upon the increase of their lumen by the dilatation of their walls. It invariably happens, however, that after the muscle has ceased to act, the flow of blood through the muscle is increased. This increase is quite independent of any alteration in the general pressure of blood in the arteries, and it occurs when an artificial stream of blood, under constant pressure, is sent through the muscle. The dilation in the muscular vessels, as indicated by the increased flow of blood, and consequent change of colour in the frog's tongue, was observed by Lépine after stimulation of the peripheral ends of the hypoglossal and glossopharyngeal nerves,[18] and the actual changes in the vessels themselves were observed microscopically by Von Frey and Gaskell.[19]

[18] Lépine, Ludwig's Arbeiten, 5ter Jahrg., 1870, p. 114.

The dilatation of muscular vessels on irritation of peripheral nerves was thus brought into a line with the dilatation noticed in the vessels of the submaxillary gland by Bernard, and in the corpora cavernosa by Eckhart. It is evident that alteration in the size of such a huge vascular tract as the muscular arteries must influence, to a great extent, the blood pressure in the arteries generally. It is equally evident that the changes induced in the condition of the blood pressure by muscular action may be of two kinds, either a rise or a fall. If the arterioles are compressed by the muscles so that the flow through them is impeded, the general blood pressure will rise. When this effect is more than counteracted by the dilatation of the arterioles themselves under nervous influence the general blood pressure will fall, for the blood will find an easy passage from the arteries into the veins through the muscles. We can thus see how readily a rise or fall in the general blood pressure may be induced by exercise of the muscles. If they contract suddenly or violently they will tend to compress the arterioles, and raise the blood pressure. If while quite easy, contraction will have little effect in compressing the arterioles, and these, becoming dilated, will allow the blood pressure to fall.

But there is still another factor which may tend to increase the blood pressure during severe muscular exertion, viz., a quickened pulse, for stimulation of the nerve fibres passing from the muscles to the central nervous system greatly accelerates the beats of the heart. In this respect stimulation of the muscular nerves differs from that of the cutaneous and visceral nerves, inasmuch as the latter tend rather to slow than to quicken the pulse. The peculiar effect of the muscular nerves upon the heart would, indeed, appear to be a provision of nature for the purpose of maintaining an exceedingly active circulation during the

[19] Von Frey, Ludwig's Arbeiten, 11ter Jahrg., 1876, p. 106; and Gaskell, *ibid.*, p. 79; and Centralb. f. die Med. Wiss., 1876, p. 557.

active calls upon nutrition which violent exertions entail. Muscular exercise, therefore, has a special tendency to raise the blood pressure in the arterial system, and consequently to increase the resistance which the left ventricle has to overcome. Moreover, in the case of the intestinal vessels there is a special provision made for preventing their contraction from causing too great a rise of arterial pressure. This consists in the depressor nerve, which passes from the heart and tends to produce dilatation of the abdominal vessels, and thus prevent any undue pressure occurring within the heart from their excessive contraction. But in the case of the muscles, we have no such nerve. Its place seems to be taken by the dilating fibres which occur in the motor nerves. As I have already said, however, their power to dilate the muscular vessels may be at first more than counteracted by mechanical compression at the commencement of exertion. Thus the blood pressure in the arteries, and the resistance which it opposes to the contraction and emptying of the ventricle, may be unduly increased at first by any effort, especially if it be sudden or severe.

As a general rule, the distension of any hollow muscular organ is attended with great pain. How great is the suffering when obstruction of the bowel prevents evacuation of its contents; or when calculi, in their passage down the gall duct or ureters, forcibly distend their walls. One of the severest tortures of the middle ages was to distend the stomach with water, and the Emperor Tiberius could imagine no more awful punishment for those whom he hated than to make them drink wine, and, at the same time, by means of a ligature, to prevent the distended bladder from emptying itself. The heart is no exception to this rule, and distension of its cavities brings on most acute physical suffering. Its inability to empty itself is a question of relative, and not of absolute power; for a strong heart may be unable to work only against enormously increased

resistance in the peripheral arterioles, while the heart, weakened by degeneration, may be unable to empty itself in face of pressure little, if at all, above the normal.

When the contractile power of the heart is not, as it is in health, considerably in excess of the resistance opposed to it in vessels, but is only nearly equal to it, a slight increase in the resistance may greatly interfere with the power of the heart to empty itself, and bring on pain varying in amount from slight uneasiness to the most intense agony in angina pectoris. This is, indeed, what we find, for a heart whose nutrition has been weakened by disease of the arteries, and consequent imperfect supply of blood to the cardiac muscle, is unable to meet any increased resistance if this should be offered to it, and pain is at once felt. In such cases, unless they be far advanced, we find, precisely as we might expect, that walking on the level usually causes no pain, but the attempt to ascend even a slight rise, by which the muscles are brought into more active exertion, brings on pain at once. Yet here again we find, as we should expect, that if the patient is able to continue walking, the pain passes off and does not return. These phenomena would be inexplicable were it not for Ludwig's observations on circulation through the muscles, but in the light of these observations everything is made perfectly intelligible. Walking on the flat, by causing no violent exertion of the muscles, produces no mechanical constriction of the vessels, and thus does not increase the blood pressure. The greater exertion of walking up a hill has this effect, but if the patient is able to continue his exertions, the increased dilatation of the vessels—a consequence of muscular activity—allows the pressure again to fall and relieves the pain.

As muscular exertion continues and the vessels of the muscles become dilated, the flow of blood from the arteries into the veins will tend to become much more rapid than usual. The pressure in the arterial system will consequently

fall, but that in the veins will become increased, and unless a corresponding dilatation occurs in the pulmonary circulation, blood will tend to accumulate in the right side of the heart, the right ventricle will be unable to empty itself completely, shortness of breath will arise, and even death may occur. At first the right side of the heart is affected, and the apex beat disappears from its normal place and is felt in the epigastrium. But the left ventricle also becomes dilated, though whether this is simply through nervous influence tending to make it act concordantly with the right, or for some other reason, it is at present impossible to say. Severe exertions, even for a few minutes, may produce this condition in healthy persons,[20] and when the exertion is over-continued it may lead to permanent mischief. More especially is this the case in young growing boys, and it is not merely foolish, it is wicked to insist upon boys engaging in games or contests which demand a long-continued over exertion of the heart, such as enforced races and paper-chases extending over several miles. Intermittent exertion, either of a single muscle or of a group of muscles, or of the whole body, appears to lead to better nutrition and increased strength and hypertrophy, but over-exertion, especially if continuous, leads to impaired nutrition, weakness, and atrophy. If we watch the movements of young animals, we find that they are often rapid, but fitful, irregular, and varied in character, instead of being steady, regular, and uniform. They are the movements of the butterfly, and not of the bee. The varied plays of childhood, the gambols of the lamb, and the frisking of the colt, are all well adapted to increase the strength of the body without doing it any injury; but if the colt, instead of being allowed to frisk at its own free will, is put in harness, or ridden in races, the energy which ought to have gone to growth is used up by the work, its nutrition is affected, its powers diminished, and

[20] Schott, Verhandl. de IX. Congresses in *Med. zu Wien*, 1890.

its life is shortened. The rules which have been arrived at by the breeders of horses ought to be carefully considered by the teachers of schools, and by the medical advisers who superintend the pupils.

In youth and middle age every organ of the body is adapted for doing more work than it is usually called upon to do. Every organ can, as it is usually termed, make a spurt if required; but as old age comes on this capacity disappears, the tissues become less elastic, the arteries become more rigid and less capable of dilating and allowing a freer flow of blood to any part, whether it be the intestine, the skin, the brain, the muscles, or the heart itself. Mere rigidity of the arteries supplying the muscles of the heart will lessen the power of extra exertion, but if the vessels be not only rigid, but diminished in calibre, the muscles of the limbs and the heart itself will be unfit even for their ordinary work, and will tend to fail on the slightest over-exertion. This fact was noticed by Sir Benjamin Brodie, who, when speaking of patients with degenerating and contracted arteries, such as lead to senile gangrene, said: "Such patients walk a short distance very well, but when they attempt more than this, the muscles seem to be unequal to the task, and they can walk no further. The muscles are not absolutely paralysed, but in a stage approaching to it. The cause of all this is sufficiently obvious. The lower limbs require sometimes a larger and sometimes a smaller supply of blood. During exercise a larger supply is wanted on account of the increased action of the muscles; but the arteries being ossified or obliterated, and thus incapable of dilatation, the increased supply cannot be obtained. This state of things is not peculiar to the lower limbs. Wherever muscular structures exist the same cause will produce the same effect. Dr. Jenner first, and Dr. Parry, of Bath, afterward published observations which were supposed to prove that the disease which is usually called

"angina pectoris" depends on ossification of the coronary arteries. . . . When the coronary arteries are in this condition they may be capable of admitting a moderate supply of blood to the muscular structure of the heart; and as long as the patient makes no abnormal exertion, the circulation goes on well enough; when, however, the heart is excited to increased action, whether it be during a fit of passion, or in running, or walking upstairs, or lifting weights, then the ossified arteries being incapable of expanding so as to let in the additional quantity of blood, which, under these circumstances, is required, its action stops and syncope ensues; and I say that this exactly corresponds to the sense of weakness and want of muscular power which exists in persons who have the arteries of the legs obstructed or ossified."[21]

But the syncope and stoppage of the heart mentioned by Brodie are not the only consequences of impaired cardiac nutrition. The heart may be still able to carry on the circulation, but the patient may suffer intense pain in the process. The outside of the heart was found by Harvey to be insensible to light touches, but the inside of the heart appears to be much more sensitive either to touch or pressure.

A knowledge of the mode of the circulation of blood through the muscles enables us to understand not only the pathology of angina pectoris, but the rationale of various methods of treating patients suffering from angina pectoris or other forms of heart disease. In most cases our object is a two-fold one—to increase the power of the heart, and to lessen the resistance it has to overcome. In some cases we require also to aid the elimination of water, which has so accumulated as to give rise to œdema of the cellular tissue, or dropsy of the serous cavities. In our endeavours to produce these beneficial changes in our patients, we

[21] ("Lectures on Pathology and Surgery," by Sir Benjamin Brodie, London, 1846, p. 360).

employ regimen, diet, and drugs, and it is evident that as in one case the condition of a patient's heart may be very different indeed from that in another, the regimen which may be useful to one may be fatal to the other. We have already seen that sudden and violent exertion may raise the blood pressure, and so lead to intense cardiac pain or to stoppage of the heart and instant death; while more gentle exercise, by increasing the circulation of the muscles, may lessen the pressure and give relief to the heart.

The methods of increasing the muscular circulation may be roughly divided into three, according as the patient lies, stands, and walks. First, absolute rest in bed with massage[22]; second, graduated movements of the muscles of the limbs and body while the patient stands still; third, graduated exercises in walking and climbing.

The second of these methods has been specially worked out by the brothers Schott, of Nauheim, and the third is generally connected with the name of Oertel.

It is obvious that in cases of heart disease where the failure is great and the patient is unable even to stand, much less walk, where breathlessness is extreme and dropsy is present, the second and third methods of treatment are inapplicable. It is in such cases that the method of absolute rest in bed, not allowing the patient to rise for any purpose whatever, hardly allowing him to feed himself or turn himself in bed, proves advantageous. The appetite is usually small, the digestion imperfect, and flatulence troublesome; and here an absolute milk diet, like that usually employed in typhoid fever, is often more serviceable, being easily taken and easily digested, while the milk sugar itself has a diuretic action, and tends to reduce dropsy. But while simple rest prevents the risk of increased arterial tension and consequent opposition to the cardiac contractions which might arise from muscular exertion, the

[22] *Practitioner*, vol. li., p. 190.

benefit which would accrue from continuous muscular exertions and increased circulation would be lost were it not that they can be supplied artificially by massage. This plan of treatment, although it has only recently been revived, was known to Harvey, "who narrates the case of a man who, in consequence of an injury—of an affront which he could not revenge—was so overcome with hatred, spite, and passion that he fell into a strange disorder, suffering from extreme compression and pain in the heart and breast, from which he only received some little relief at last when the whole of his chest was pummelled by a strong man, as the baker kneads dough." [23]

This was a very rough form of massage, but the same kneading movements which Harvey described have been elaborated into a complete system, more especially by Ling in Sweden, and made widely known in America and this country by Weir-Mitchell, and Playfair. One might naturally expect that kneading the muscles would increase the circulation through them in somewhat the same way as active exercise, but, to the best of my knowledge, no actual experiments existed to prove this, and I accordingly requested my friend and assistant, Dr. Tunnicliffe, to test the matter experimentally. The method employed was, in the main, the same as that devised by Ludwig, and employed by Sadler and Gaskell under his direction. The results were that, during the kneading of a muscle the amount of venous blood which issued from it was sometimes diminished and sometimes increased; that just after the kneading was over the flow was diminished, (apparently, from the blood accumulating in the muscle) and this diminution was again succeeded by a greatly increased flow exactly corresponding to that observed by Ludwig and his scholars. The clinical results are precisely what one would expect from increased circulation in the muscles, and cases apparently hopeless sometimes recover most wonderfully under this treatment.

[23] "The Works of W. Harvey," Sydenham Society's edition, p. 128

For patients who are stronger, so that confinement to bed is unnecessary, and who yet are unable to take walking exercise, Schott's treatment is most useful, and it may be used as an adjunct to the later stages of the treatment just described, or as a sequel to it. Here the patient is made to go through various exercises of the arms, legs, and trunk with a certain amount of resistance, which is applied either by the patient himself setting in action the opposing muscles, or by an attendant, who gently resists every movement made by the patient, but graduates his resistance so as not to cause the least hurry in breathing, or the least oppression of the heart. Perhaps the easiest way of employing graduated resistance is by the ergostat of Gärtner, which is simply an adaptation of the labour crank of prisons, where the number of turns of a wheel can be regulated in each minute, and the resistance, which is applied by a brake, may be graduated to an ounce. The objection to it is the uniformity of movement and its wearisome monotony.

Oertel's plan of gradually walking day by day up a steeper and steeper incline, and thus training the cardiac muscle is well adapted for strong persons, but when applied injudiciously, may lead, just like hasty or excessive exertion, to serious or fatal results. In Schott's method stimulation of the skin by baths is used as an adjunct, and this may tend to slow the pulse as already mentioned. But in all these plans the essence of treatment is the derivation of blood through a new channel, that of the muscular vessels; and the results in relieving cardiac distress and pain may be described in the same words which Harvey employs in reference to diseases of the circulation: "How speedily some of these diseases that are even reputed incurable are remedied and dispelled as if by enchantment."[24]

There is yet another consequence of the circulation to which Harvey has called attention, although only very

[24] "The Works of William Harvey," Sydenham Soc. edition, p. 141.

briefly, which has now become of the utmost importance, and that is the admixture of blood from various parts of the body. After describing the intestinal veins, Harvey says: "The blood returning by these veins and bringing the cruder juices along with it, on the one hand from the stomach, where they are thin, watery, and not yet perfectly chylified; on the other, thick and more earthy, as derived from the fæces, but all pouring into this splenic branch, are duly tempered by the admixture of contraries."[25]

Harvey's chemical expressions are crude, for chemistry as a science only began to exist about a century and a half after Harvey's death, yet the general idea which he expresses in the words which I have just quoted is wonderfully near the truth.

Two of the most important constituents of the blood are chloride of sodium and water. Chloride of sodium is a neutral salt, but during digestion both it and water are decomposed in the gastric glands, and hydrochloric acid is poured into the stomach, while a corresponding amount of soda is returned into the blood, whose alkalinity increases *pari passu* with the acidity of the stomach. Part of this alkali is excreted in the urine, so that the urine during digestion is often neutral or alkaline. Possibly some of it passes out through the liver in the bile, through the pancreas and intestinal glands into the intestine, where, again mixing with the acid chyle from the stomach, neutralisation takes place, so that neutral and comparatively inactive chloride of sodium is again formed from the union of active alkali and acid. But it is most probable that what occurs in the stomach occurs also in the other glands, and that the liver, pancreas and intestine, do not merely pour out the excess of alkali resulting from gastric digestion, but that these glands also decompose neutral salts, pouring the alkali out through their ducts, and returning the acid into the blood.

[25] "The Works of William Harvey," Sydenham Soc. edition, p. 75.

We are now leaving the region of definite fact and passing into that of fancy, but the fancies are not entirely baseless, and may shew in what directions we may search out and study the secrets of nature by way of experiment. For what is apparently certain in regard to the decomposition of chloride of sodium in the stomach, and probably in the case of neutral salts in the pancreas and intestine, is also probable in that important, though as yet very imperfectly known, class of bodies which are known as zymogens. Just as we have in the stomach an inactive salt, so we have also an inactive pepsinogen, which, like the salt, is split up in the gastric glands, and active pepsine is poured into the stomach. But is pepsine the only active substance produced? Has no other body, resulting from the decomposition of pepsinogen, been poured into the blood while the pepsine passed into the stomach? Has the inactive pepsinogen not been split up into two bodies active when apart, inactive when combined? May it not be fitly compared, as I have said elsewhere, to a cup or glass, harmless while whole, but yielding sharp and even dangerous splinters when broken, although these may again be united into a harmless whole?[26]

This question at present we cannot answer, but in the pancreas there is an indication that something of the kind takes place, for Lépine has discovered that while this gland pours into the intestine a ferment which converts starch into sugar, it pours through the lymphatics into the blood another ferment which destroys sugar. Whether a similar occurrence takes place in regard to its other ferments in the pancreas, or in the glands of the intestine, we do not know. Nor do we yet know whether the same process goes on in the skin, and whether the secretion of sweat, which is usually looked upon as its sole function, bears really a relationship to cutaneous activity similar to that which the secretion of bile bears to the functions of the liver. There are indications that such is the case, for when the skin is

[26] *Practitioner*, vol. xxxv., August, 1885.

varnished, not only does the temperature of the animal rapidly sink, but congestion occurs in internal organs, and dropsy takes place in serous cavities, while in extensive burns of the skin rapid disintregration of the blood corpuscles occurs. It is obvious that if this idea be at all correct, a complete revolution will be required in the views we have been accustomed to entertain regarding the action of many medicines. In the case of purgatives and diaphoretics, for example, we have looked mainly at the secretions poured out after their administration for an explanation of their usefulness, whereas it may be that the main part of the benefit that they produce is not due to the substances liberated through the secretions which they cause to be poured out, but to those which are returned from the intestine and skin into the circulating blood.

How important an effect the excessive admixture of juices from one part of the animal body with the circulating blood may have, was shown in the most striking way by Wooldridge. The juice of the thyroid gland is harmless so long as it remains in the gland, and is probably useful when it enters the blood in small quantities in the ordinary course of life. Yet he found that if this juice be injected directly into the vessels it will cause the blood to coagulate almost instantaneously and kill the animal as quickly as a rifle bullet. But what is powerful for harm is, likewise, powerful for good, and the administration of thyroid juice in cases of myxœdema is one of the most remarkable therapeutic discoveries of modern times.

Since the introduction by Corvisart of pepsine as a remedy in dyspepsia, digestive ferments have been largely employed to assist the stomach and intestine in the performance of their functions, but very little has been done until lately in the way of modifying tissue changes in the body by the introduction of ferments derived from solid organs.

For ages back, savages have eaten raw hearts and other organs of the animals which they have killed, or the

enemies they have conquered, under the belief that they would thereby obtain increased vigour or courage; but the first definite attempt to cure a disease by supplying a ferment from a solid non-glandular organ of the body was, I believe, made in Harvey's own hospital by the use of raw meat in diabetes.[27]

It was not, however, until Brown-Séquard recommended the use of testicular extract that the attention of the profession became attracted to the use of extracts of solid organs. Since then extract of thyroid, extract of kidney, extract of supra renal capsule have been employed; but even yet they are only upon their trial, and the limits of their utility have not yet been definitely ascertained.

Another therapeutic method has been recently introduced which bids fair to be of the utmost importance—viz., the treatment of disease by antitoxins. The discovery by Pasteur of the dependence of many diseases upon the presence of minute organisms may be ranked with that of Harvey, both in regard to the far-reaching benefits which it has conferred upon mankind and for the simplicity of its origin. The germ of all his discoveries was the attempt to answer the apparently useless question, "Why does a crystal of tartaric acid sometimes crystallise in one form and sometimes in another?" From this germ sprung his discovery of the nature of yeast, and of those microbes which originate fermentation, putrefaction, and disease.

These minute organisms, far removed from man as they are in their structure and place in nature, appear in some respects to resemble him in the processes of their growth and nutrition. They seem, indeed, to have the power of splitting up inactive bodies into substances having a great physiological or chemical activity. From grape sugar, which is comparatively inert, they produce carbonic acid and alcohol, both of which have a powerful physiological

[27] *Brit. Med. Jour.*, February 21, 1874, p. 221 *et seq.*

action. From inert albumen they produce albumoses having a most powerful toxic action, and to the poisonous properties of these substances attention was for a while alone directed. But it would appear that at the same time as they produce poisons they also form antidotes, and when introduced into the living organism they give rise to the production of these antidotes in still greater quantity than when cultivated without the body.

The plan of protection from infective diseases, which was first employed by Jenner in small-pox, is now being extended to many other diseases, and the protective substances which are formed in the body, and their mode of action, are being carefully investigated. The introduction of either pathogenic microbes or of toxic products appears to excite in the body a process of tissue-change by which antitoxins are produced, and these may be employed either for the purpose of protection or cure. By the use of antitoxins tetanus and diphtheria appear to be deprived of their terrible power.

But it seems probable that a similar result may be obtained by the introduction of certain tissue juices into the general circulation, for it was shown by Wooldridge that thyroid juice has the power of destroying anthrax poison. Increase of the circulation in certain organs will almost certainly increase their tissue change, will throw their juices or the products of their functional activity into the general circulation, and thus influence the invasion or progress of disease. As I have already mentioned, we are able to influence the circulation in muscles both by voluntary exertion and by massage, and we should expect that both of these measures would influence the constituents of the blood generally. Such, indeed, appears to be the case, for J. K. Mitchell[28] has found that after massage the number of blood corpuscles in the circulation is very considerably increased. We can thus understand why

[28] *American Journal of Medical Science*, May, 1894.

exercise either of the body or its parts may increase its power to resist infective diseases.

Had time allowed it, I had intended to discuss the modifications of the heart and vessels by the introduction of remedies into the circulation, the power of drugs to slow or strengthen, to quicken or weaken the power of the heart, to contract or relax the arterioles, to raise or lower the blood pressure, to relieve pain or to remove dropsy; but to do this would require time far exceeding that of a single hour. Moreover, the methods and results of such research were admirably expounded to the College by Dr. Leech in his Croonian lecture, and I have therefore thought I should be better fulfilling the wish of Harvey that the orator of the year should exhort the Fellows and Members of the College to search out the secrets of nature by way of experiment by directing their attention to some fields of research which have received at present little attention, but promise results of great practcal value.

Lastly, I have to exhort you to continue in mutual love and affection among ourselves; and it seems to me that the best way of doing this is to direct your attention to the examples of Harvey and of our late President, whose death we deplore to-day. They were beloved by their fellows while they lived, their loss was lamented when they died, and they have left behind them an example not only of goodness, but of courage. Harvey, seated speechless in his chair, distributing rings and parting gifts to his friends while awaiting the approach of death; and Andrew Clark, steadfastly determining to continue at work and die in harness, in spite of the hæmoptysis which seemed to threaten a speedy death, afford us noble examples which ought to encourage us to follow the directions of the venerable Longfellow, who, taking the organ Harvey studied to symbolise such courage as Harvey and Clark showed, says:

"Let us then be up and doing
With a heart for any fate,
Still achieving, still pursuing,
Learn to labour and to wait."

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Brunton, (Sir) Thomas
Lauder
Modern developments
of Harvey's work

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